

Applicant: Boldogh et al.

Serial No.: 10/691,330

Filed: October 22, 2003

Title: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS INHIBITORS OF APOPTOSIS AND OTHER CELLULAR DAMAGE

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### **Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

### **Listing of Claims**

1. (Currently amended) A method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof;

wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog inhibits apoptosis in a cell;

and wherein the apoptosis inhibitor inhibits apoptosis in the cell.

2. (Original) The method of claim 1 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

3. (Original) The method of claim 1 wherein the cell is a mammalian cell.

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4. (Original) The method of claim 3 wherein the cell is a human cell.
5. (Currently amended) The method of claim 1 wherein the inhibitor is ~~a constituent peptide of colostrinin~~.
6. (Currently amended) The method of claim [[5]] 1 wherein the inhibitor is a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPP (SEQ ID NO:8), ~~VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPPFKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34)~~, and combinations thereof.
7. (Currently amended) A method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof, ~~wherein:~~  
wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LQTPQPLLQVMMEPQGD (SEQ ID NO:2),

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DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLV (SEQ ID NO:4),  
DLEMPVLVPEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6),  
VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

~~the active analog is an active analog of a constituent peptide of colostrinin selected from the group of SEQ ID NO:1 through SEQ ID NO:34;~~

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin; a constituent peptide of colostrinin selected from the group consisting of MOPPPPLP (SEQ ID NO:1) LQTPQPLLOVMMPEQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLV (SEQ ID NO:4), DLEMPVLVPEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein-diacetate;

and wherein the apoptosis inhibitor inhibits apoptosis in the cell.

8. (Original) The method of claim 7 wherein the apoptosis is due to DNA damage.
9. (Original) The method of claim 7 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.
10. (Original) The method of claim 7 wherein the cell is a mammalian cell.
11. (Original) The method of claim 10 wherein the cell is a human cell.
12. (Currently amended) A method for protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group

**Amendment and Response**

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consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof;

wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4), DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DOPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLVLP (SEQ ID NO:4), DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein-diacetate;

and wherein the compound protects the cell against DNA damage.

13. (Original) The method of claim 12 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.
14. (Original) The method of claim 12 wherein the cell is a mammalian cell.
15. (Original) The method of claim 14 wherein the cell is a human cell.

**Amendment and Response**

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16. (Withdrawn) A method for reducing the toxic effect of  $\beta$ -amyloid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof.

17. (Withdrawn) The method of claim 16 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

18. (Withdrawn) The method of claim 16 wherein the cell is a mammalian cell.

19. (Withdrawn) The method of claim 18 wherein the cell is a human cell.

20. (Withdrawn) A method for reducing the toxic effect of retinoic acid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof.

21. (Withdrawn) The method of claim 20 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

22. (Withdrawn) The method of claim 20 wherein the cell is a mammalian cell.

23. (Withdrawn) The method of claim 22 wherein the cell is a human cell.

24. (Cancel)